DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

October 29, 2014

SIEMENS HEALTHCARE DIAGNOSTICS, INC.
FÁTIMA PACHECO
REGULATORY CLINICAL AFFAIRS SPECIALIST
511 BENEDICT AVENUE
TARRYTOWN NY 10591

Re: K142864
Trade/Device Name: ADVIA Centaur C-peptide (CpS) Master Curve Material (MCM)
ADVIA Centaur Insulin (IRI) Master Curve Material (MCM)
Regulation Number: 21 CFR 862.1660
Regulation Name: Single (Specified) Analyte Controls (Assayed and Unassayed)
Regulatory Class: Class I, Reserved
Product Code: JJX
Dated: September 30, 2014
Received: October 01, 2014

Dear Ms. Fátima Pacheco:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical

device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
*See PRA Statement below.*

510(k) Number *(if known)*
k142864

Device Name
ADVIA Centaur® C-peptide Master Curve Material (MCM)

Indications for Use *(Describe)*
The ADVIA Centaur® C-peptide (CpS) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur C-peptide assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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**FOR FDA USE ONLY**

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
*See PRA Statement below.*

510(k) Number *(if known)*
k142864

Device Name
ADVIA Centaur® Insulin Master Curve Material (MCM)

Indications for Use *(Describe)*
The ADVIA Centaur® Insulin (IRI) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur insulin assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

**PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.**

**FOR FDA USE ONLY**

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

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*PRAStaff@fda.hhs.gov*

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## 510(k) Summary

**Introduction:** According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

**The assigned 510(k) Number: k142864**

| | |
|---|---|
| **1. Applicant Information** | Siemens Healthcare Diagnostics Inc. |
| **Mailing Address:** | 511 Benedict Avenue<br>Tarrytown, NY 10591 USA |
| **Contact Person:** | Fatima Pacheco<br>Regulatory Clinical Affairs Specialist |
| **Phone Number:** | (914) 524-2450 |
| **Fax Number:** | (914) 524-3579 |
| **E-mail Address:** | fatima.pacheco@siemens.com |
| **Date Prepared:** | October 23, 2014 |
| **2. Device Name** | |
| **Proprietary Name:** | **ADVIA Centaur® C-peptide (CpS) Master Curve Material** |
| **Measurand:** | Quality Control materials for ADVIA Centaur CpS assay |
| **Type of Test:** | Master Curve Material (MCM) for ADVIA Centaur CpS assay |
| **Regulation Section:** | 21 CFR 862.1660, Quality Control Material |
| **Classification:** | Class I Reserved |
| **Products Code:** | JJX – Single (Specified) Analyte Controls (Assayed and Unassayed) |
| **Panel:** | Clinical Chemistry (75) |
| **3. Predicate Device Name** | Elecsys C-Peptide CalCheck 5 |
| **Predicate 510(k) No:** | K100810 |
| **4. Device Description:** | ADVIA Centaur® C-peptide Master Curve Material is an *in vitro* diagnostic product containing various levels of C-peptide spiked in citric acid buffer with casein and preservatives. Each set contains ten levels (MCM1–10); ready-to-use 1.0 mL per level. MCM1 contains no analyte. The MCMs assigned values are lot-specific of target values 0.0, 0.14, 0.25, 0.55, 1.05, 2.05, 4.00, 8.00, 16.0, 32.5 ng/mL. |
| **5. Intended Use:** | See Indications for Use Statement below: |

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| | |
|---|---|
| **Indication for Use:** | The ADVIA Centaur® C-peptide (CpS) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur C-peptide assay. |
| **Special Conditions for Use Statement(s):** | For prescription use only |
| **Special Instrument Requirements:** | ADVIA Centaur® Systems<br>A description of the ADVIA Centaur system is documented in K971418. Subsequent modifications to the instrument have been reviewed and cleared in K032525 and K041133. |
| **6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:** | A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur CpS MCM is substantially equivalent to the predicate device as summarized in **Table 1**. |

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***Table 1:*** *Substantial Equivalence Comparison*

| **SIMILARITIES** | | |
|---|---|---|
| | **Candidate Device** | **Predicate Device** |
| **Item** | ADVIA Centaur CpS MCM | Elecsys C-Peptide CalCheck 5 |
| **Intended Use** | The ADVIA Centaur C-peptide (CpS) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur C-peptide assay. | The Elecsys C-Peptide CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the serum and plasma assay range established by the Elecsys C-Peptide reagent on the indicated Elecsys and cobas e immunoassay analyzers. |
| **Analyte** | C-peptide | Same |
| **Use** | Multiple Use | Same |
| **Storage** | 2–8°C | Same |
| **DIFFERENCES** | | |
| **Form** | Liquid | Lyophilized |
| **Matrix** | Citric acid buffered casein | HEPES buffered equine serum matrix |
| **Levels** | 10 | 5 |
| **Stability** | **Unopened** – Stable when stored unopened at 2–8°C for 12 months.<br>**Opened** – Stable on-board for 4 hours. | **Unopened** – Stable at 2–8°C for 15 months.<br>**Reconstituted** – Stable for 4 hours at 20–25°C. |

## 7. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

## 8. Performance Characteristics

### 8.1 Performance Studies

#### 8.1.1 *Stability Studies*

Stability studies were conducted to support the shelf life of unopened and opened ADVIA Centaur CpS MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur CpS MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur CpS MCM:

- Real Time/Shelf Life (unopened) Stability
- On-Board Stability

*Real time shelf-life studies (unopened):* Test CpS MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 3 months, 7 months, 9 months, 12 months, and 13 months. At each time point 3 replicates were run for each MCM level. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results. Acceptance criteria for the real-time stability study were met up to the 13 month time point, which supports a shelf-life claim of 12 months. Unopened storage shelf-life is indicated by the expiration date on the MCM vial label.

*On-board Stability:* Pooled aliquots of test CpS MCMs in sample cups were stored on the ADVIA Centaur system and measured at time point T=0, 2, 4 and 5 hours. On-board stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results. Acceptance criteria for the on-board stability study were met up to 5 hours, which supports the on-board stability claim for 4 hours. At each time point 3 replicates were run for each MCM level.

*Stability Acceptance Criteria*

The stability specifications acceptance criteria for the ADVIA Centaur CpS MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 must be ≤ 0.15 ng/mL dose; MCM2, the % dose recovery must be within 85 to 115%; MCM3–10, the % dose recovery must be within 88 to 112% calculated back to Day 0 and/or no adverse trends.

- On-Board: The dose recovery for MCM1 must be ≤ 0.15 ng/mL dose; MCM2, the % dose recovery must be within 85 to 115%; MCM3–10, the % dose recovery must be within 88 to 112% calculated to T=0.

### 8.1.2 *Value Assignment*

The ADVIA Centaur CpS MCMs are value assigned using assigned reference standards. The assigned reference standards are prepared using CpS stock and are standardized against World Health Organization (WHO) IS 84/510 reference material. The MCMs are manufactured using qualified materials and measurement procedures.

MCM1–10 are run in 3 replicates across two ADVIA Centaur instruments using two reagent kit lots, run twice on each instrument for a total of 24 replicates per MCM level. MCM9 is run diluted 1:2 using the MCM1 level. The average MCMs dose values are generated using the master curve standard calibration. The MCM10 dose value is calculated by multiplying the MCM9 dose value by 2. Three levels of commercially available controls and two levels in-house controls are used to verify acceptable value assignment runs and validate the results. The two in-house controls are diluted using diluents buffer to satisfy a 0.40–0.60 ng/mL and 12.0–18.0 ng/mL concentration of C-peptide respectively. The average dose for each in-house and commercial control from the value assignment runs are expected to be within +/-10% of the assigned targets and the ratio of in-house control RLUs to the Standard 1 RLUs (reaction counts) must be within 25–65. The average dose values obtained are the new MCM dose values (target). The new MCM doses must fall within the target range for each MCM level as outlined in **Table 1.**

**Table 1: CpS MCM Target and Target Ranges**

| MCM Level | Target (ng/mL) | Target Range (ng/mL) |
|---|---|---|
| MCM1 | 0.00 | < 0.06 |
| MCM2 | 0.14 | 0.10–0.18 |
| MCM3 | 0.25 | 0.20–0.30 |
| MCM4 | 0.55 | 0.40–0.70 |
| MCM5 | 1.05 | 0.80–1.30 |
| MCM6 | 2.05 | 1.70–2.40 |
| MCM7 | 4.00 | 3.50–4.50 |
| MCM8 | 8.00 | 7.00–9.00 |
| MCM9 | 16.0 | 14.0–18.0 |
| MCM10 | 32.5 | 30.0–35.0 |

### 8.1.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges are established per % interval as below.

| MCM Level | % Interval |
|---|---|
| MCM1 | N/A |
| MCM2 | 30 |
| MCM3 | 30 |
| MCM4 | 30 |
| MCM5 | 30 |
| MCM6 | 25 |
| MCM7 | 25 |
| MCM8 | 25 |
| MCM9 | 25 |
| MCM10 | 25 |

The target for MCM1 is assigned a 0.0 dose. There is no statistical method used to assign the 0.0 dose. The MCM1 range is always assigned as "< " less than 0.09 ng/mL. MCM1 is analyte-free citric acid buffer comprising of only the matrix and preservatives

If the above % interval creates an overlapping range for any two MCM levels, the ranges are adjusted using the following process: The low range value for the next MCM level is set at +0.01 of the high range value of the previous MCM level.

Lot-specific assigned target and assigned ranges are provided in the ADVIA Centaur CpS MCM lot-specific value sheet in the example provided in **Table 2.**

***Table 2:*** *Lot-specific CpS MCM Target and Assigned Target and Range*

| MCM level | Target (ng/mL) | Assigned Target (ng/mL) | Assigned Range (ng/mL) |
|---|---|---|---|
| MCM1 | 0.00 | 0.00 | < 0.09 |
| MCM2 | 0.14 | 0.17 | 0.12–0.22 |
| MCM3 | 0.25 | 0.26 | 0.23–0.34 |
| MCM4 | 0.55 | 0.61 | 0.43–0.79 |
| MCM5 | 1.05 | 1.07 | 0.80–1.39 |
| MCM6 | 2.05 | 2.28 | 1.71–2.85 |
| MCM7 | 4.00 | 4.40 | 3.30–5.50 |
| MCM8 | 8.00 | 8.91 | 6.68–11.1 |
| MCM9 | 16.0 | 16.6 | 12.5–20.8 |
| MCM10 | 32.5 | 33.2 | 24.9–41.5 |
| **Assay Range** | 0.05–30 ng/mL | | |

#### 9.2.4 *Traceability*

The ADVIA Centaur CpS assay is traceable to World Health Organization (WHO) IS 84/510 reference material. Assigned values for master curve standards, calibrators, and MCMs are traceable to this standardization. The CpS MCMs are manufactured using qualified materials and measurement procedures.

## 10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

## 11. Conclusion

The ADVIA Centaur CpS Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Elecsys C-Peptide CalCheck 5. Based on the testing completed and the comparisons with the predicate device, the ADVIA Centaur CpS MCM does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

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## 510(k) Summary

**Introduction:** According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

**The assigned 510(k) Number: k142864**

| | |
|---|---|
| **1. Applicant Information** | |
| **Mailing Address:** | Siemens Healthcare Diagnostics Inc.<br>511 Benedict Avenue<br>Tarrytown, NY 10591 USA |
| **Contact Person:** | Fatima Pacheco<br>Regulatory Clinical Affairs Specialist |
| **Phone Number:** | (914) 524-2450 |
| **Fax Number:** | (914) 524-3579 |
| **E-mail Address:** | fatima.pacheco@siemens.com |
| **Date Prepared:** | October 23, 2014 |
| **2. Device Name** | |
| **Proprietary Name:** | **ADVIA Centaur® IRI Master Curve Material** |
| **Measurand:** | Quality Control materials for ADVIA Centaur IRI assay |
| **Type of Test:** | Master Curve Material (MCM) for ADVIA Centaur IRI assay |
| **Regulation Section:** | 21 CFR 862.1660, Quality Control Material |
| **Classification:** | Class I Reserved |
| **Products Code:** | JJX – Single (Specified) Analyte Controls (Assayed and Unassayed) |
| **Panel:** | Clinical Chemistry (75) |
| **3. Predicate Device Name** | Elecsys Insulin CalCheck 5 |
| **Predicate 510(k) No:** | K101075 |
| **4. Device Description:** | ADVIA Centaur® Insulin Master Curve Materials is an *in vitro* diagnostic product containing various levels of insulin in buffered saline with casein, potassium thiocyanate (3.89%), sodium azide (<0.1%), and preservatives. Each set contains ten levels (MCM1–10); ready-to-use 1.0 mL per level. MCM1 contains no analyte. The IRI MCMs assigned values are lot-specific of target values: 0.0, 2.5, 4.5, 10.0, 20.0, 39.0, 79.0, 158, 225, and 300 mU/L. |
| **5. Intended Use:** | See Indications for Use Statement below: |
| **Indication for Use:** | The ADVIA Centaur® Insulin (IRI) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur Insulin assay. |

| | |
|---|---|
| **Special Conditions for Use Statement(s):** | For prescription use only |
| **Special Instrument Requirements:** | ADVIA Centaur® Systems<br>A description of the ADVIA Centaur system is documented in K971418. Subsequent modifications to the instrument have been reviewed and cleared in K032525 and K041133. |
| **6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:** | A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur IRI MCM is substantially equivalent to the predicate device as summarized in **Table 1**. |

***Table 1:*** *Substantial Equivalence Comparison*

| SIMILARITIES | | |
|---|---|---|
| | **Candidate Device** | **Predicate Device** |
| **Item** | ADVIA Centaur IRI MCM | Elecsys Insulin CalCheck 5 |
| **Intended Use** | The ADVIA Centaur Insulin (IRI) MCM is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur Insulin assay. | The Elecsys Insulin CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the assay range established by the Elecsys Insulin reagent on the indicated Elecsys and **cobas e** immunoassay analyzers. |
| **Analyte** | Insulin | Same |
| **Use** | Multiple Use | Same |
| **Storage** | 2–8°C | Same |
| **DIFFERENCES** | | |
| **Matrix** | Buffered saline with casein, potassium thiocyanate and azide | Bovine Serum matrix |
| **Form** | Liquid | Lyophilized |
| **Levels** | 10 | 5 |
| **Stability** | **Unopened** – Stable when stored unopened at 2–8°C for 11 months.<br>**Opened** – Stable on-board for 8 hours. | **Unopened** – Stable at 2–8°C for 18 months.<br>**Opened (Reconstituted)** – Stable for 4 hours at 20–25°C. |

## 7. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

## 8. Performance Characteristics

### 8.1 Performance Studies:

#### 8.1.1 *Stability Studies*

Stability studies were conducted to support the shelf life unopened material for the ADVIA Centaur IRI MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur IRI MCM Instructions for Use.
The following stability studies were performed for ADVIA Centaur IRI MCM:

- Real Time/Shelf Life (unopened) Stability
- On-Board Stability

*Real time shelf-life studies (unopened):* Test IRI MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 3 months, 7 months, 9 months and 12 months. At each time point 3 replicates were run for each MCM level. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results. Acceptance criteria for the real-time stability study were met up to the 12 month time point, which supports a shelf-life claim of 11 months. Unopened storage shelf-life is indicated by the expiration date on the vial label.

*On-board Stability:* Pooled aliquots of test IRI MCMs in sample cups were stored on the ADVIA Centaur system and measured at time point T= 0, 2, 4, 6, 8, and 9 hours. Acceptance criteria for the on-board stability study were met up to 9 hours, which supports the on-board stability claim for 8 hours. At each time point 3 replicates were run for each MCM level.

*Stability Acceptance Criteria*

The stability specifications acceptance criteria for the ADVIA Centaur IRI MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 must be ≤ 1.5 mU/L dose; MCM2, the % dose recovery must be within 85 to 115%; MCM3–10, the % dose recovery must be within 88 to 112% calculated to Day 0 and/or no adverse trends.
- On-Board: The dose recovery for MCM1 must be ≤ 1.5 mU/L dose; MCM2, the % dose recovery must be within 85 to 115%; MCM3–10, the % dose recovery must be within 88% to 112% calculated to Time=0.

### 8.1.2 *Value Assignment*

The ADVIA Centaur IRI MCMs are value assigned using assigned reference standards. The assigned reference standards are prepared using IRI stock and are standardized against World Health Organization (WHO) 1st IRP 66/304 reference material. The MCMs are manufactured using qualified materials and measurement procedures.

MCM1–10 are run in replicates of three across two ADVIA Centaur instruments using two reagent kit lots, run twice on each instrument for a total of 24 replicates per MCM level. MCM10 is also run diluted 1:2 using the MCM1 level as diluent. The average MCMs dose values are generated using the master curve standard calibration. Two lots of commercially available controls (3 levels) are used to verify acceptable value assignment runs and validate the results. The average dose for each commercial control from the value assignment runs are expected to be within +/- 10% of the assigned targets and the coefficient of variation value from each commercial control is to be within 10%. The average dose values obtained are the new MCM dose values (target). The MCM10 dose value (target) is the average dose value of the neat and diluted samples. The new MCM doses must fall within the target range for each MCM level as outlined in **Table 1**.

**Table 1: Insulin MCM Target and Target Ranges**

| MCM Level | Target (mU/L) | Target Range (mU/L) |
|---|---|---|
| MCM1 | 0.00 | < 0.50 |
| MCM2 | 2.50 | 2.00–3.00 |
| MCM3 | 4.50 | 4.00–5.00 |
| MCM4 | 10.0 | 9.00–11.0 |
| MCM5 | 20.0 | 18.0–22.0 |
| MCM6 | 39.0 | 35.0–43.0 |
| MCM7 | 79.0 | 71.0–87.0 |
| MCM8 | 158 | 142–173 |
| MCM9 | 225 | 200–250 |
| MCM10 | 330 | 300–360 |

The target for MCM1 is assigned a 0.0 dose. There is no statistical method used to assign the 0.0 dose. The MCM1 range is always assigned as "<" less than 2.05 mU/L. MCM1 is analyte-free buffered saline comprising of only the matrix and preservatives.

If the above % interval creates an overlapping range for any two MCM levels, the ranges are adjusted using the following process: The low range value for the next MCM level is set at +0.01 of the high range value of the previous MCM level.

### 8.1.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges are established per % interval as below.

| MCM Level | % Interval |
|---|---|
| MCM1 | N/A |
| MCM2 | 20 |
| MCM3 | 20 |
| MCM4 | 20 |
| MCM5 | 20 |
| MCM6 | 20 |
| MCM7 | 20 |
| MCM8 | 18 |
| MCM9 | 15 |
| MCM10 | 12 |

Lot-specific target and assigned values are provided in the ADVIA Centaur IRI MCM lot-specific value sheet in the example provided in **Table 2.**

***Table 2:*** *Lot-specific IRI MCM Target and Assigned Values*

| MCM Level | Target Values (mU/L) | Assigned Values (mU/L) | Assigned Range (mU/L) |
|---|---|---|---|
| MCM1 | 0.00 | 0.00 | < 2.05 |
| MCM2 | 2.50 | 2.52 | 2.06–3.02 |
| MCM3 | 4.50 | 4.73 | 3.78–5.68 |
| MCM4 | 10.0 | 10.0 | 8.00–12.0 |
| MCM5 | 20.0 | 18.9 | 15.1–22.7 |
| MCM6 | 39.0 | 38.3 | 30.6–46.0 |
| MCM7 | 79.0 | 72.3 | 57.8–86.8 |
| MCM8 | 158 | 168 | 138–198 |
| MCM9 | 225 | 234 | 199–269 |
| MCM10 | 330 | 322 | 283–361 |
| **Assay Range** | 0.50–300 mU/L | | |

### 9.2.4 *Traceability*

The ADVIA Centaur Insulin assay is standardized against World Health Organization (WHO) 1$^{st}$ IRP 66/304. Assigned values for master curve standards, calibrators and MCMs are traceable to this standardization. The IRI MCMs are manufactured using qualified materials and measurement procedures.

**10. Proposed Labeling**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**11. Conclusion**

The ADVIA Centaur IRI Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Elecsys Insulin CalCheck 5. Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur IRI Maser Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.